

## REMARKS

The Office Action mailed July 10, 2002, has been received and reviewed. Claims 1, 3-11, 13-44, 46, 48-64, 66-74 and 105-107 are currently pending in the application, all of which were rejected. Applicant respectfully requests reconsideration of the referenced application for the reasons set forth below.

### Rejections Maintained

#### **Obviousness Rejections under 35 U.S.C. § 103(a)**

##### Standard for Obviousness Rejections

M.P.E.P. § 706.02(j) sets forth the standard for a Section 103(a) rejection:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002). The factual inquiry whether to combine references must be thorough and searching and based on objective evidence of record. *Id.* Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *Id.* Even when the level of skill in the art is high, the Office must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination. *Id.* In other words, the Office must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious. *Id.* When

the Office relies on what it asserts to be general knowledge to negate patentability, that knowledge must be articulated and placed on the record. *Id.* at 1345. The Office cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies. *Id.*

Obviousness Rejection Based on Isaka in view of Overton

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 as being assertedly unpatentable over Isaka et al. (U.S. Patent 5,482,598) in view of Overton et al. (U.S. Patent 5,611,846). Applicant respectfully traverses this rejection, as below set forth.

The Office relies on Isaka as teaching a chromatograph apparatus that includes a silicon substrate having a *single* porous microchannel formed therein. *Paper No. 16*, pages 4-5. The Office asserts that Isaka differs from the claimed invention only “in failing to teach forming at least two porous microchannels in the silicon substrate.” *Paper No. 16*, p. 5. The Office relies on Overton as disclosing that the gas chromatograph may include *two* different parallel columns, as depicted in FIG. 2(b) and discussed at column 9, lines 30-46. *Id.*

Independent claim 1 recites a sample separation apparatus that includes a substrate having matrices formed therein. The matrices comprise at least two distinct, unconnected porous regions that extend at least partially across the substrate. The sample separation apparatus of claim 1 also includes at least one detector fabricated on the substrate and associated with at least one of the at least two porous regions.

Independent claim 30 recites a separation apparatus comprising at least two distinct, unconnected capillary columns formed in a substrate, each of which comprises a porous matrix. The separation apparatus of claim 30 also includes a detector fabricated on the substrate and associated with at least one of the at least two porous regions.

Independent claim 51 recites a miniature chromatograph comprising a substrate having porous matrices, which have a plurality of pores, formed in the substrate that comprise at least two distinct, unconnected capillary columns.

Independent claim 64 recites an analyte detection apparatus comprising a silicon substrate with matrices formed therein, the matrices comprising at least two distinct, unconnected porous columns continuous with a surface of the silicon substrate.

Applicant respectfully submits there are several reasons why the Office has not established a *prima facie* case of obviousness with respect to any of the rejected claims.

***Reasonable Expectation of Success***

The obviousness rejection of independent claims 1, 30, 51, and 64 is improper because there would not have been a reasonable expectation of success in combining the cited references as proposed at the time the present invention was made. The Office asserts that one of ordinary skill in the art would have a reasonable expectation of success in incorporating the multiple columns of Overton into the miniaturized chromatograph apparatus of Isaka because Overton taught that multiple columns may be incorporated into chromatograph apparatuses. The Office alleges that this suggests that the use of multiple columns in chromatograph apparatuses is well within ordinary skill. *Paper No. 18*, p. 6. However, “[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.” *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Overton’s teachings that multiple conventional tubular columns can be incorporated in miniaturized chromatographic devices find no application in chromatograph devices formed in silicon, gallium arsenide, or indium phosphide substrates. Success with multiple conventional tubular columns would not translate into success with columns formed in silicon, gallium arsenide, or indium phosphide substrates because the structural differences in the two types of columns are great.

Taken together and considered as a whole, the teachings of Isaka and Overton are incompatible because they deal with vastly different approaches to miniaturized chromatographic devices. If one of ordinary skill in the art of fabricating miniaturized chromatographs in a silicon substrate were to follow the teachings of Overton, she or he would be lead, if at all, to incorporate *interconnected* columns, not two or more distinct, unconnected porous regions, as recited in the subject claims.

When considered in its entirety, Overton teaches that its columns are interconnected to facilitate the selection of the column through which the sample is conveyed. *Overton*, FIG. 2(b); col. 9, line 43, through col. 10, line 18. Therefore, any modification of Isaka to include the teachings of Overton would include interconnected columns. However, the matrices of claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 are distinct, unconnected porous regions and, therefore, are not interconnected.

In addition, Overton discloses a multiple column apparatus having pneumatic valves at the interconnections between columns. The pneumatic valves of Overton could not be used to interconnect porous columns formed in a silicon, gallium arsenide, or indium phosphide substrate.

Overton thus teaches away from the claimed invention by teaching interconnected, conventional tubular columns and pneumatic valves at the interconnections between columns.

#### ***Teaching or Suggestion of All Claim Limitations***

The obviousness rejection of independent claims 1, 30, 51, and 64, and claims depending therefrom, is also improper because the proposed combination of Isaka and Overton does not teach or suggest every limitation of the subject claims.

Each of independent claims 1, 30, 51, and 64 recites a separation apparatus that comprises a substrate with matrices formed therein. The matrices comprise at least two distinct, unconnected porous regions that extend at least partially across the substrate.

Neither Isaka nor Overton teaches or suggests a substrate comprising two or more distinct, unconnected porous matrices. Rather, Isaka teaches a miniaturized chromatograph including a *single* porous column formed in a silicon substrate. And Overton teaches a miniaturized gas chromatograph device that includes multiple *interconnected, conventional tubular* chromatography columns. Thus, the columns of Overton are not matrices formed in a substrate, nor do the columns of Overton include distinct, unconnected regions. Therefore, the asserted combination of Isaka and Overton lacks any teaching or suggestion of a separation apparatus with distinct, unconnected porous regions.

Applicant thus respectfully submits the proposed combination of Isaka and Overton fails to teach or suggest all the limitations of the subject claims. Withdrawal of the obviousness rejection of independent claims 1, 30, 51, and 64 is thus respectfully requested on this ground.

***Suggestion or Motivation to Combine Reference Teachings***

The obviousness rejection of independent claims 1, 30, 51, and 64 is also improper because the Office has not made the requisite particularized findings of a suggestion or motivation in the evidence of record to select and combine the references as proposed. *See, e.g.*, *In re Lee*, 277 F.3d 1338, 1343-1345 (Fed. Cir. 2002). Rather than pointing to objective evidence of record providing the requisite suggestion or motivation to combine the cited references as proposed, the Office simply states that the rejection “is based on an obvious combination of the teachings of Isaka and Overton.” *Paper No. 22*, p. 7. It is respectfully submitted that applicant’s own disclosure is the only evidence of record that suggests the desirability of the claimed invention.

In each Office Action treating this rejection, the Office has made essentially the same statement concerning an alleged suggestion or motivation to combine the references as proposed, to wit:

“Overton specifically taught that multiple columns in various configurations for different intended applications can be incorporated into miniaturized chromatograph devices suggesting that fabrication and use of multiple columns in separation chromatographs is well within ordinary skill.” *Paper No. 20*, p. 9; *see also Paper No. 18*, p. 6; *Paper No. 16*, p. 6.

Although the Office never has explicitly identified a specific passage in Overton supportive of the above-quoted statement, applicant believes the Office is referring to the statement in Overton that “[t]he basic design of the novel chromatograph allows a wide variety of specific instrument configurations, to fit particular intended uses” (*Overton*, col. 9, lines 30-32), to which the Office imputes an alleged suggestion that “fabrication and use of multiple columns in separation chromatographs is well within ordinary skill.” *Paper No. 20*, p. 9.

Applicant respectfully submits that this logical leap is unwarranted, particularly as it relates to the claimed invention. Overton’s statement that his invention allows a wide variety of configurations suggests nothing with respect to the level of ordinary skill in the art of separation

column devices formed in silicon, gallium arsenide, or indium phosphide substrates, which is completely different from the level of ordinary skill in the art of conventional tubular chromatographs.

Applicant respectfully submits there is no suggestion or motivation in the objective evidence of record to combine Isaka's teaching of a single column formed in a silicon substrate with Overton's teaching of multiple conventional tubular columns that are interconnected. One of ordinary skill in the art having knowledge of the teachings of Isaka and Overton would not have been motivated to combine the references in such a way as to develop an apparatus with a plurality (at least two) distinct, unconnected porous regions or columns, as recited in independent claims 1, 30, 51, and 64.

Overton is silent as to chromatograph columns comprising porous silicon. Furthermore, while the above-quoted statement in Overton may be considered relevant to the reasonable expectation of success analysis, it is inapposite with respect to the analysis of a suggestion or motivation to select and combine the cited references as proposed. In other words, the fact that reference teachings *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916, F.2d 680 (Fed. Cir. 1990). What is lacking in the Office's obviousness analysis is a *reason* why one of ordinary skill would be motivated to select and combine the references as proposed.

The Office's attention is respectfully directed to FIG. 6 and the accompanying discussion in Overton, where it is plainly evident that Overton's discussion of chromatograph columns, including the columns used in Overton's invention, refers to conventional tubular columns. *Overton*, FIG 6; col. 10, lines 24-25; col. 16, lines 35-36. Overton is silent as to the desirability or efficacy of miniaturized chromatograph columns comprising porous silicon formed in a substrate. Therefore, it is respectfully submitted that the statement in Overton the Office relies upon as a suggestion that it is "well within ordinary skill" to fabricate and use multiple columns can only refer to conventional tubular columns, not porous silicon regions formed in a substrate, as in the rejected claims.

Applicant respectfully submits the Office has not identified any evidence of record supportive of a suggestion or motivation to select and combine Isaka and Overton as proposed. Thus, it is respectfully asserted that the Office must be relying either on applicant's own

disclosure or some unarticulated general knowledge in the art in reaching the conclusion that the cited references should be selected and combined as proposed. These are improper bases for an obviousness rejection. Accordingly, it is respectfully submitted the Office has not established a *prima facie* case of obviousness with respect to the subject claims.

#### *Nonanalogous Art*

Applicant respectfully submits that the Office's reliance on Overton is also improper because Overton is nonanalogous art. *See, e.g.*, MPEP § 2141.01(a). In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the invention was concerned. *In re Oetiker*, 977 F.2d 1443, 1446 (Fed. Cir. 1992).

It is evidence of nonanalogy that Overton, Isaka, and the claimed invention are classified differently by the Office for searching purposes. MPEP § 2141.01(a). While Isaka is currently classified in classes 428/409; 205/656; 205/666; 216/2; 438/960, Overton is currently classified in classes 96/102; 73/23.36; 73/23.41; 73/23.42; 95/82; 95/86; 95/87; 96/104; 96/105.

Applicant's elected invention is classified in class 210/659, as indicated in the Restriction Requirement made in the Office Action mailed July 21, 1999. *Paper No. 3*, p. 2. It is thus apparent, at least for Office searching purposes, that Overton is nonanalogous art as to both Isaka and the present invention.

More persuasive indicia of nonanalogy include the substantial structural differences that exist between Overton and Isaka and the claimed invention. *In re Ellis*, 476 F.2d 1370, 1372 (CCPA 1973). Applicant respectfully submits that Overton's teachings with respect to conventional tubular column gas chromatograph devices are not reasonably pertinent to chromatograph column devices fabricated on a silicon, gallium arsenide, or indium phosphide substrate, as recited in the subject claims and as taught by Isaka.

One of ordinary skill in the art seeking to solve the problems associated with multiple separation columns that are formed in a silicon, gallium arsenide, or indium phosphide substrate, as recited in the subject claims, would not look to the art of miniaturized conventional tubular column gas chromatograph devices because the design and manufacture of these respective devices are entirely unrelated. That is, Overton's teachings with respect to miniature tubular

column gas chromatographic devices of conventional configuration with multiple, interconnected columns have no application whatsoever to the art of multiple, unconnected separation columns fabricated in a silicon, gallium arsenide, or indium phosphide substrate. Compare, for example, Overton's FIG. 6, illustrating his column assembly schematically, and Overton's FIG. 2(b), illustrating his multiple column apparatus, with Isaka's FIGS. 1A through 3, illustrating his microchannel element fabricated in silicon substrate and with FIGS. 1 through 6 of the present application, illustrating multiple, unconnected porous matrices formed in a substrate. Applicant respectfully submits the conventional tubular multi-column device Overton teaches is so different in its structure and fabrication from the silicon substrate column devices of Isaka and the present invention that Overton is not reasonably pertinent to the problems solved by the present invention, namely, multiple columns formed in a substrate, such that one of ordinary skill would have looked to Overton for a solution to the problems solved by the subject matter recited in the pending claims. Accordingly, applicant respectfully submits the Office's reliance on Overton is misplaced and, therefore, respectfully requests withdrawal of the rejection on this ground.

Therefore, independent claims 1, 30, 51, and 64 are not obvious, and claims 3-5, 7, 9-11, 13, 16, 18-20, 25, 29, 31-32, 34, 38, 39, 43, 46, 48-50, 52-53, 56, 69-71 and 73 depending therefrom are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

In summary, the Office has not established a *prima facie* case of obviousness with respect to independent claims 1, 30, 51, and 64 because (1) the Office has failed to establish a reasonable expectation of success of the proposed combination, (2) the Office has not made particular findings, based on the evidence of record, as to the reason the ordinarily skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed, (3) the combination proposed by the Office does not teach or suggest all the limitations of independent claims 1, 30, 51, and 64, and claims depending therefrom, and (4) the Office's reliance on Overton is improper because it is nonanalogous art.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Swedberg

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 8, 26-28, 35-37, and 66-68 as being assertedly unpatentable over Isaka in view of Overton as applied

to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above and further in view of Swedberg et al. (U.S. Patent 5,571,410). Applicant respectfully traverses this rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except the use of antibody or antigen as the capture substrate for the miniaturized chromatograph. *Paper No. 16*, p. 13.

The Office relies on Swedberg “for the teaching of a capture function that can be incorporated into miniaturized chromatographic devices wherein antibodies, antigens, and other biological affiants are immobilized into the column matrix for capturing biological components and separating them from other components in the sample.” *Paper No. 22*, p. 8. The Office further notes that Swedberg (at col. 10) makes reference to “complementary microchannels” (more than one channel). *Paper No. 22*, p. 9. The Office relies on this fleeting reference to microchannel in the plural in support of its contention that Swedberg “does provide a suggestion to fabricate multiple microchannels in a chromatographic device, if desired.” *Id.*

#### ***Suggestion or Motivation to Combine Reference Teachings***

Applicant respectfully submits that the Office has not made the requisite showing of a suggestion or motivation to select and combine Swedberg with Isaka and Overton in the manner proposed. On the contrary, Swedberg expressly teaches away from chromatograph column devices formed in silicon substrates. *See, e.g., Swedberg*, col. 7, line 53, through col. 8, line 4; col. 4, lines 54-59; col. 6, lines 13-20. Swedberg states: “It is a primary object of the present invention to provide a miniaturized column device laser-ablated in a substantially planar substrate, wherein said substrate is comprised of a material selected to avoid the inherent chemical activity and pH instability encountered with silicon and prior silicon dioxide-based device substrates.” *Swedberg*, col. 4, lines 54-59. Swedberg also teaches away from the proposed combination in that Swedberg’s chromatograph matrices are formed of material foreign to the substrate, which is loaded into the columns formed in the substrate. *See, e.g., Swedberg*, col. 27, lines 44-61; col. 33, lines 31-34. Thus, one of ordinary skill in the art would not have been motivated to combine Swedberg’s teaching of a capture function incorporated in a

miniaturized chromatograph device with Isaka and Overton to produce at least two distinct, unconnected porous matrices formed in a substrate, as recited in claims 8, 26-28, 35-37, and 66-68.

Assuming, for the sake of argument, that Swedberg does teach multiple microchannels in a chromatographic device, Swedberg nevertheless fails to teach or suggest that these multiple microchannels are distinct and unconnected, as recited in the subject claims. Since Swedberg does not cure the previously discussed deficiencies, claims 8, 26-28, 35-37, and 66-68 are not obvious over the combination of Isaka, Overton, and Swedberg.

Finally, as set forth above, the proposed combination of Isaka and Overton does not render obvious claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73. Thus, claims 8 and 26-28 (dependent from nonobvious independent claim 1), 35-37 (dependent from nonobvious independent claim 30), and 66-68 (dependent from nonobvious independent claim 64) are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Accordingly, withdrawal of the obviousness rejection of claims 8, 26-28, 35-37, and 66-68 is respectfully solicited.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Miura

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 14-15, 17, 21, 40-41, 44, and 54-55 as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above, and in further view of Miura et al. (U.S. Patent No. 5,132,012). Applicant respectfully traverses this rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except for incorporating a field effect transistor detector, memory device, and controls in the apparatus. *Paper No. 16*, p. 6.

The Office relies on Miura as disclosing:

“a miniaturized sample separator in the form of a liquid chromatograph comprising an analyzing chip in which the capillary flowpath is formed in a substrate and a field effect transistor detector disposed downstream of the capillary. The substrate is made of silicon and further has an insulative membrane

formed of silicon dioxide. Both the column for separation and the field effect transistor detector are formed integrally with the substrate. After the silicon oxide layer has been formed on the capillary groove, a stationary phase is formed. A valve is connected to a first end of the flow path in the sample application area (sample introduction pipe) where a sample is selectively introduced into the flow path. A separation carrier solution (carrier gas/vacuum source) is fed under pressure by a feed pump and then discharged from a drain after having passed through the flow path. Miura *et al.* further teach a sealing element (seal plate) such as borosilicate glass for sealing the opening portion of the groove portion to define the flow passage for a liquid sample. The liquid chromatograph also comprise[s] a memory (control) device and an output device such as a data processor which is connected to the detector for detecting separated constituents. Figures 4A and 4B illustrate an electrical conductivity detector which comprise[s] voltage application and current detection components, i.e. electrodes. Figure 9 shows a schematic view of the overall flow passage of the liquid chromatograph.”

*Paper No. 16, pp. 6-7.*

It is respectfully submitted that the single, substrate-bound open column of Miura does not cure the deficiencies of the proposed combination of Isaka and Overton. Specifically, Miura does not provide any suggestion or motivation to one of ordinary skill in the art combine the single, substrate-bound porous column of Isaka with the multiple, interconnected conventional tubular columns of Overton to produce the invention of any of claims 14-15, 17, 21, 40-41, 44, and 54-55. Moreover, one of ordinary skill in the art would not have a reasonable expectation that the proposed combination of references would be successful, nor does the proposed combination teach or suggest the all limitations of the subject claims. Finally, the Office’s reliance on Overton is improper because Overton is nonanalogous art. Applicant therefore respectfully submits that claims 14-15, 17, 21, 40-41, 44, and 54-55 are not rendered obvious by the proposed combination of Isaka, Overton, and Miura.

Claims 17 and 44 are also allowable because the combination of Isaka, Overton, and Miura, as proposed by the Office, does not teach or suggest a memory device *on a substrate*, as recited in the subject claims. None of the cited references teaches or suggests a memory device. Thus, the proposed combination does not teach or suggest a memory device *on a substrate*, as recited in claims 17 and 44.

Claims 21 and 41 are further allowable because the proposed combination of Isaka, Overton, and Miura does not teach or suggest a vacuum source in operative communication with

a porous region. Neither Isaka nor Overton includes any teaching or suggestion of a vacuum source in communication with a porous region, which would be analogous to the columns thereof. The teachings of Miura are limited to the use of positive pressure to facilitate the movement of a sample through the column. *Miura*, col. 10, lines 1-34.

The Office contends that claims 21 and 41 do not exclude positive pressure, but the fact remains that none of Isaka, Overton, nor Miura teaches or suggests that a vacuum source may be operatively communicate with a column thereof. It is difficult to conceive how the limitation of claims 21 and 41 reciting “a vacuum source”, which is inherently a source of negative pressure, can be taught or suggested by a reference that teaches only positive pressure. Thus, it is respectfully submitted the proposed combination fails to teach all the limitations of the subject claims.

Further, as set forth above, the proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious. Thus, claims 14, 15, 17, 21 (dependent from nonobvious independent claim 1), 40, 41, 44 (dependent from nonobvious independent claim 30), and 54 and 55 (dependent from nonobvious independent claim 51) are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Accordingly, withdrawal of the obviousness rejection of claims 14-15, 17, 21, 40-41, 44, and 54-55 is respectfully solicited.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Wang

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 21 and 41 as being unpatentable over Isaka in view of Overton as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above and further in view of Wang et al. (U.S. Patent 5,663,488). Applicant respectfully traverses the rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except for integration of a migration facilitator into the separation chromatograph. *Paper No. 16*, p. 8.

The Office relies on Wang as teaching “a migration facilitator comprising exemplary pumps to facilitate migration of the samples through the claimed column.” *Paper No. 22*, p. 10.

The addition of the teachings of Wang does not cure the deficiencies of the proposed combination of Isaka and Overton. Specifically, Wang does not provide any additional suggestion or motivation to combine the single, substrate-bound porous column of Isaka with the multiple, interconnected conventional tubular columns taught by Overton to produce the invention recited in claims 21 and 41, provide a reasonable expectation that the combination of Isaka and Overton would be successful, or teach or suggest the claim limitations that are lacking from the combination of Isaka and Overton (*i.e.*, at least two distinct, unconnected porous regions (matrices) formed in a substrate). Finally, the Office’s reliance on Overton is improper because Overton is nonanalogous art.

Claims 21 and 41 are further allowable because the proposed combination of Isaka, Overton, and Wang does not teach a vacuum source operatively in communication with an end of the chromatography column, as recited in the subject claims. In contrast to the vacuum sources recited in claims 21 and 41, which are in operative communication with a porous region to facilitate migration of a sample therethrough, the vacuum of Wang is used to vary the pressure within a chamber in which the separation column device has been placed so as to thermally isolate the chamber from the environment. *See, e.g., Wang*, col. 1, line 63 through col. 2, line 4; col. 2, lines 29-41. Because Wang’s vacuum source applies equal pressure to all parts of the separation column device placed in the vacuum chamber, Wang’s vacuum source cannot facilitate migration of samples through a column on the device. It is, therefore, respectfully submitted the proposed combination does not teach or suggest all the limitations of the subject claims.

Finally, the proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 21 (dependent from nonobvious independent claim 1) and 41 (dependent from nonobvious independent claim 30) are not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

It is, thus, respectfully submitted that the proposed combination of Isaka, Overton, and Wang does not render claims 21 or 41 obvious under 35 U.S.C. § 103(a). Applicant, hence,

respectfully submits the Office has not established a *prima facie* case of obviousness with respect to the subject claims. Accordingly, withdrawal of the obviousness rejection of claims 21 and 41 is respectfully solicited.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Northrup

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 22-24 and 42 as being unpatentable over Isaka in view of Overton as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above and further in view of Northrup et al. (U.S. Patent 5,882,496). Applicant respectfully traverses the rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except for the migration facilitator comprising electrodes disposed into the porous region of the chromatograph. *Paper No. 16*, p. 11.

The Office relies on Northrup as teaching “electrodes within or adjacent porous membranes which are used to control flow of electrically charged biochemical species such as in electrophoresis, i.e. negative electrode is formed at one end (inlet) of a column and a positive electrode is formed at an opposite end of a column, thereby forming microelectrophoresis channels.” *Paper No. 22*, p. 11. The Office further relies on Northrup as exemplifying multiple microelectrophoresis channels. *Id.*

Applicant respectfully submits the addition of the teachings of Northrup does not cure the deficiencies discussed above concerning the proposed combination of Isaka and Overton. Specifically, Northrup does not provide any suggestion or motivation to one of ordinary skill in the art to combine the single, substrate-bound porous column of Isaka with the multiple, interconnected, conventional tubular columns of Overton, provide a reasonable expectation that the combination of Isaka and Overton would be successful, or teach or suggest the claim limitations that are lacking from the combination of Isaka and Overton. Nor does Northrop remedy the fact that the teachings of Overton are not analogous to the subject matter recited in the subject claims.

Therefore, it is respectfully submitted that the proposed combination of Isaka, Overton, and Northrup does not render any of claims 22-24 or 42 obvious.

Finally, the proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 22-24 (dependent from nonobvious independent claim 1) and 42 (dependent from nonobvious independent claim 30) are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Accordingly, Applicant respectfully requests withdrawal of the obviousness rejection of claims 22-24 and 42.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Northrup and Sunzeri

The Office maintained the previous rejection under 35 U.S.C. § 103(a) of claims 6, 57-62 and 72 as being assertedly unpatentable over Isaka in view of Overton as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above and further in view of Northrup and Sunzeri (U.S. Patent 5,536,382). Applicant respectfully traverses the rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except for an electrophoretic apparatus comprising porous silicon columns and incorporating a control column into a separation device comprising porous silicon. *Paper No. 20*, p. 7.

The Office relies on Northrup as teaching “electrodes within or adjacent porous membranes which are used to control flow of electrically charged biochemical species such as in electrophoresis, i.e. negative electrode is formed at one end (inlet) of a column and a positive electrode is formed at an opposite end of a column, thereby forming microelectrophoresis channels.” *Paper No. 22*, p. 12. The Office further relies on Northrup as exemplifying multiple microelectrophoresis channels. *Id.*. And the Office relies on Sunzeri “for the teaching of incorporating internal or external standards into a column chromatograph.” *Paper No. 22*, p. 12.

Applicant respectfully submits that neither the multiple porous silicon electrophoretic columns of Northrup nor the electrophoretic-media-filled capillary tubes used in Sunzeri cure the deficiencies discussed above concerning the proposed combination of the single, substrate-bound porous column of Isaka and the multiple, interconnected, conventional tubular columns of Overton. Furthermore, the Office has not identified any proper suggestion or motivation in any of the references to select and combine Isaka, Overton, Northrup, and Sunzeri, as proposed, demonstrated that Northrup or Sunzeri would give one of ordinary skill in the art any reason to believe that the asserted combination would be successful, or remedied that fact that the teachings of Overton are not analogous to the subject matter recited in the subject claims.

Finally, as set forth above, the proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious. Applicant respectfully submits claims 57-62 also are not rendered obvious by the proposed combination for the same reasons. Claims 6 (dependent from nonobvious independent claim 1) and 72 (dependent from nonobvious independent claim 64) are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Applicant thus respectfully submits the Office has not established a *prima facie* case of obviousness with respect to the subject claims. Withdrawal of the obviousness rejection of claims 6, 57-62 and 72 is, therefore, respectfully solicited.

### New Grounds of Rejection

#### **Anticipation Rejections under 35 U.S.C. § 102(e)**

#### Standard for Anticipation Rejections

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). And the elements of the prior art reference must be arranged as required by the subject claim. *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990); *See generally MPEP* § 2131.

Anticipation Rejection Based on U.S. Patent No. 6,225,159 to Thakur

Claims 105-107 were newly rejected under 35 U.S.C. § 102(e) as being anticipated by Thakur, U.S. Patent No. 6,225,159 (“Thakur ‘159”). Applicant respectfully traverses this rejection, as set forth below.

The Office relies on Thakur ‘159 as disclosing an ultrasmall flow channel device (trench capacitor) comprising a flow inlet and a flow channel (elongate trench) formed on a surface of a silicon, gallium arsenide, or indium phosphide substrate which comprises silicon matrix and wherein a selected layer of the amorphous silicon is converted to hemispherical grain (HSG) silicon. *Paper No. 22*, p. 4.

Applicant respectfully disagrees that Thakur ‘159 describes an ultrasmall flow channel device comprising a “flow inlet” connected to a “flow channel”, as recited in rejected claims 105-107. On the contrary, the trench capacitor structure described in Thakur ‘159 would not permit flow of analytes through it because a capacitor dielectric is formed generally conformally over the bottom electrode and a doped generally conformal poly layer is then formed over the cell dielectric and serves as a common capacitor cell plate to an entire array of finished trenched capacitors. *Thakur ‘159*, Abstract; col. 7, lines 39-45. Thakur’s trench capacitor 410 is expressly described as an open trench within which, in some embodiments, HSG is formed. However, Thakur’s trench capacitor is neither expressly nor inherently described to comprise a flow inlet connected to the trench, as recited in the subject claims. Moreover, Thakur ‘159 does not expressly or inherently describe a flow channel. Rather, the description of Thakur ‘159 is limited to capacitor trenches, which are known in the relevant art to be confined to small discrete areas. Thus, the capacitor trenches of Thakur ‘159 do not comprise channels.

Further, with respect to claims 106 and 107, Thakur neither expressly nor inherently describes a stationary phase of any sort (claim 106), silicon oxide (claim 107) or otherwise, disposed on the HSG silicon formed in the trench.

In view of the foregoing, applicants respectfully submit Thakur ‘159 neither expressly nor inherently describes each and every limitation of claims 105-107 and, as a result, fails to anticipate the subject claims. Applicants therefore respectfully solicit withdrawal of the rejection based on Thakur ‘159.

Anticipation Rejection Based on U.S. Patent No. 6,126,847 to Thakur

Claims 105-107 were newly rejected under 35 U.S.C. § 102(e) as being anticipated by Thakur, U.S. Patent No. 6,126,847 (“Thakur ‘847”). Applicant respectfully traverses this rejection, as set forth below.

The Office relies on Thakur ‘847 as disclosing “ultrasmall flow channels formed in silicon, gallium arsenide, or indium phosphide devices comprising a flow inlet and a flow channel on a surface of the substrate which includes silicon oxide and wherein HSG is selectively etched and formed thereon.” *Paper No. 20*, p. 4.

Applicant respectfully disagrees that Thakur ‘847 describes an ultrasmall flow channel device comprising a “flow inlet” connected to a “flow channel”, as in rejected claims 105-107. The container structure 16 of Thakur ‘847 is expressly described as an open-topped structure on the walls of which HSG is formed. *See, e.g., Thakur ‘847*, FIGS. 1-3; col. 3, line 56 through col. 5, line 26. However, Thakur’s container structure 16 is neither expressly nor inherently described to have a flow inlet connected thereto, as recited in the subject claims.

Further, with respect to claims 106 and 107, Thakur ‘847 neither expressly nor inherently describes a stationary phase of any sort (claim 106), silicon oxide (claim 107) or otherwise, disposed on the HSG formed in the trench.

In view of the foregoing, applicants respectfully submit Thakur ‘847 neither expressly nor inherently describes each and every element of claims 105-107 and, accordingly, fails to anticipate the subject claims. Applicants therefore respectfully solicit withdrawal of the rejection based on Thakur ‘847.

Obviousness Rejection Based on Isaka in view of Overton and further in view of Northrup and Crenshaw

Claims 33, 63, and 74 were newly rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38-39, 43, 46, 48-53, 56, 64, 69-71, and 73 above and further in view of Northrup and Crenshaw et al. (U.S. Patent 5,726,085). Applicant respectfully traverses the rejection, as set forth below.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton assertedly teach all the limitations of the subject claims except that the porous silicon matrix comprises hemispherical grain (HSG) silicon. *Paper No. 22*, p. 5. The teachings of Northrup, as relied upon by the Office, are as discussed above.

The Office relies on Crenshaw as disclosing “a capacitor wherein a thin layer of HSG is deposited over a doped polysilicon region and then etched using etch chemistry, to increase surface area.” *Paper No. 22*, p. 6. The Office states its case of obviousness as follows:

“It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the porous silicon matrix disclosed by Isaka or Northrup as modified by Overton, with HSG as taught by Crenshaw because Crenshaw taught using HSG on capacitors to increase surface area and Northrup specifically taught that porosity in silicon structures increases surface area in miniaturized separation flow channels such as in his electrophoresis device or the microchannel separation device disclosed by Isaka and HSG. *Paper No. 22*, p. 6.

Crenshaw describes forming hemispherical grained silicon 70 on the surface of charge storage nodes 64, which protrude from the substrate. *Crenshaw*, FIGS. 4C, 4D; col. 3, lines 34-59. Crenshaw’s charge storage *nodes* 64 are not flow *channels*, as recited in the subject claims. Further, whereas the claimed porous matrices are formed *in* the substrate, Crenshaw’s charge storage nodes 64 are protruding structures formed *over* the substrate. *Compare Crenshaw*, FIG. 4C with FIG. 8 of the present application.

The addition of the teachings of Northrup and Crenshaw fails to cure the deficiencies discussed above in relation to the proposed combination of Isaka and Overton. Namely, the proposed combination fails to teach or suggest the limitation reciting at least two distinct, unconnected columns formed in a silicon, gallium arsenide, indium phosphide substrate, as recited in the subject claims. Accordingly, the proposed combination fails to teach or suggest all the limitations of the subject claims and does not render the claimed invention obvious. Additionally, the Office has not shown that Northrup or Sunzeri provide any suggestion or motivation that is missing from Isaka and Overton to combine the teachings of these referendes, demonstrated that Northrup or Sunzeri would give one of ordinary skill in the art any reason to

believe that the asserted combination would be successful, or remedied that fact that the teachings of Overton are not analogous to the subject matter recited in the subject claims.

Applicant further respectfully submits the Office has not made the requisite findings based on evidence of record as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *See In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002). The above quoted statement of the Office's case for obviousness is, at best, an "obvious to try" rationale, which is not a proper basis for an obviousness rejection. *See In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). As discussed above, Crenshaw teaches a method of fabricating a *capacitor over* a substrate, which is completely inapposite to the claimed apparatuses comprising porous matrices formed *in a* substrate, so one of ordinary skill would not have been motivated to combine Crenshaw's teachings with respect to HSG with the teachings of Isaka, Overton, and Northrup, as proposed. Applicant thus respectfully submits the Office has not established a *prima facie* case of obviousness in the absence of the requisite showing of a suggestion or motivation in the evidence of record to select and combine the cited references in the manner proposed. Withdrawal of the rejection is respectfully requested on this basis.

Further, Applicant respectfully disagrees with the Office's assertion that HSG is an obvious variation of porous silicon used in separation devices. The Office cites no objective evidence of record to support the proposition that HSG is an obvious variation of porous silicon. Crenshaw, the only one of the cited references that includes any teachings with respect to HSG, makes no reference whatsoever to porous silicon. And Crenshaw's HSG layer is taught to be disposed on the outer surface of a capacitor structure protruding from a substrate rather than within matrices formed within a substrate, as recited in the subject claims. Further, neither Isaka nor Northrup, which both disclose use of porous silicon, include any discussion of HSG or suggestion that HSG is an obvious variation of porous silicon. Applicant hence respectfully submits there is no suggestion or motivation to combine Crenshaw's teachings with the other cited references to produce the claimed invention.

Finally, as set forth above, the proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious. Claim 63 is not obvious for the same reasons. Claims 33 (dependent from

nonobvious independent claim 30) and 74 (dependent from nonobvious independent claim 64) are likewise not obvious. *In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Therefore, applicant respectfully submits the Office has not established a *prima facie* case of obviousness with respect to claims 33, 63, and 74 and respectfully requests withdrawal of the rejection on this basis.

### CONCLUSION

Claims 1, 3-11, 13-44, 46, 48-64, 66-74 and 105-107 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved expeditiously by a telephone interview, she is respectfully invited to contact applicant's attorney of record.

Respectfully submitted,



Brick G. Power  
Registration Number 38,581  
Attorney for Applicant  
TRASKBRITT, PC  
P.O. Box 2550  
Salt Lake City, Utah 84110  
Telephone: (801) 532-1922

BGP/SGH/djp  
Date: October 7, 2002

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